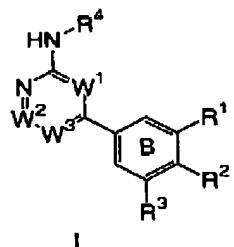


Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936

AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

1. (Previously presented) A compound of formula I:



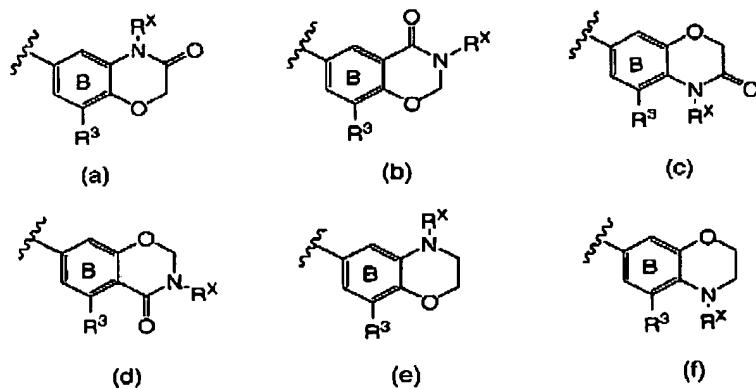
or a pharmaceutically acceptable salt thereof, wherein:

W¹ is nitrogen or CH, W² is nitrogen or C-(U)_pR^U, and W³ is nitrogen or C-(V)_qR^V;
 p and q are each independently 0 or 1;
 R^U and R^V are each independently R or Ar¹;
 U and V are each independently a bond or a C₁₋₆ alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRRRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR;
 each occurrence of R is independently hydrogen or an optionally substituted C_{1-C4} aliphatic, or two R bound to the same nitrogen atom are optionally taken together with the nitrogen atom to form a 3-7 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 additional heteroatoms independently selected from nitrogen, oxygen, or sulfur;
 Ar¹ is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or

Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936

sulfur; wherein Ar¹ is optionally substituted with m independent occurrences of Z-R⁵; wherein m is 0-5, Z is a bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of Z are optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; and each occurrence of R⁵ is independently hydrogen, an optionally substituted aliphatic, heteroaliphatic, aryl or heteroaryl group, halogen, NO₂, CN, OR, SR, N(R)₂, NRCOR, NRCON(R)₂, NRCO₂R, COR, CO₂R, OCOR, CON(R)₂, OCON(R)₂, SOR, SO₂R, SO₂N(R)₂, NRSO₂R, NRSO₂N(R)₂, COCOR, or COCH₂COR;

R¹ and R² are taken together and fused to ring B to form a heterocyclic moiety selected from one of formulae (a) through (f):



wherein each occurrence of R^X is independently hydrogen, QR, or Q_nAr¹; n is zero or one; and Q is an optionally substituted C₁-₄ alkylidene chain wherein one methylene unit of Q is optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR;

R³ is hydrogen, halogen, QR, Q_nCN, Q_nNO₂, or Q_nAr¹; and

R⁴ is Ar¹, or T-Ar¹;

Applicants: Randy S. Bethel et al.
Application No.: 10/700,936

wherein T is a C₁₋₂ alkylidene chain wherein one methylene unit of T is optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRRNCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR.

2. (Previously presented) The compound of claim 1, wherein R¹ and R² taken together form the heterocyclic moiety of formula (a) and R^X is hydrogen or optionally substituted C₁₋₆ aliphatic.

3. (Original) The compound of claim 1, wherein R^X is hydrogen, methyl, ethyl, propyl, n-butyl, tert-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, C₁₋₆alkyl substituted with N(R)₂, or C₁₋₆alkyl substituted with Ar¹.

4. (Original) The compound of claim 1, wherein R^X is hydrogen, methyl, or C₁₋₂alkyl substituted with a group selected from optionally substituted phenyl, pyridyl, morpholino, piperidinyl, or piperazinyl.

5. (Original) The compound of claim 1, wherein R³ is hydrogen, halogen, QR or QAr¹, wherein Q is a C₁₋₃ alkylidene chain wherein one methylene unit of Q is optionally replaced by -O-, -S-, -NHCO-, or -NR-, and Ar¹ is an optionally substituted 5-6 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

6. (Original) The compound of claim 1, wherein R³ is hydrogen, OH, OCH₃, OCH₂CH₃, NHCOMe, NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, O(CH₂)₂morpholin-4-yl, O(CH₂)₂NH₂, O(CH₂)₂NH(C₁₋₄ aliphatic), O(CH₂)₂N(C₁₋₄ aliphatic)₂, Br, Cl, or F.

7. (Original) The compound of claim 1, wherein R³ is hydrogen.

Applicants: Randy S. Bethel et al.
Application No.: 10/700,936

8. (Original) The compound of claim 1, wherein R⁴ is a 6-membered saturated, partially unsaturated, or aryl ring having 0-3 nitrogens, a 9-10 membered bicyclic aryl ring having 0-2 nitrogen atoms, or a 5 membered heteroaryl ring having 2-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein each ring is optionally substituted.

9. (Original) The compound of claim 1, wherein R⁴ is optionally substituted phenyl, cyclohexyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, thiazolyl, thiadiazolyl, pyrazolyl, isoxazolyl, indazolyl, or benzimidazolyl.

10. (Original) The compound of claim 1, wherein R⁴ is an optionally substituted phenyl group.

11. (Original) The compound of claim 8, wherein each occurrence of Z is independently a bond or a C₁₋₄ alkylidene chain wherein one methylene unit of Z is optionally replaced by -O-, -S-, -SO₂-, or -NH-; and each occurrence of R⁵ is independently hydrogen, C₁₋₆ aliphatic, halogen, NO₂, OR, N(R)₂, or optionally substituted phenyl, pyridyl, or pyrimidinyl.

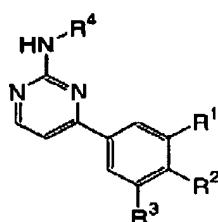
12. (Previously presented) The compound of claim 8, wherein each occurrence of ZR⁵ is independently Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF₃, NH₂, phenyl, benzyl, benzyloxy, OH, methylenedioxy, SO₂NH₂, CONH₂, CO₂Me, phenoxy, O-pyridinyl, SO₂phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF₃-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, and fluorophenoxy.

13. (Original) The compound of claim 1, wherein (U)_pR^U and (V)_qR^V are each independently hydrogen, halogen, NO₂, CN, OR, SR or N(R)₂, or C₁₋₄aliphatic optionally substituted with oxo, OR, SR, N(R)₂, halogen, NO₂ or CN.

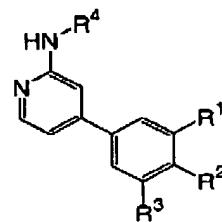
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936

14. (Original) The compound of claim 1, wherein $(U)_p R^U$ and $(V)_q R^V$ are each independently hydrogen, Me, OH, or OMe.

15. (Original) The compound of claim 1, wherein W^1 is N or CH and compounds have the structure of Formula Ia or Ib:



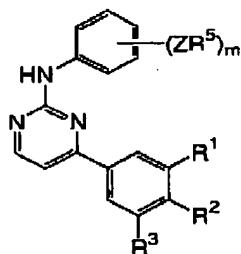
Ia



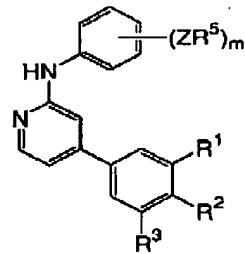
Ib

or a pharmaceutically acceptable salt thereof.

16. (Previously presented) The compound of claim 15, wherein R^4 is an optionally substituted phenyl group and compounds have the structure of Formula IIa or IIb:



IIa

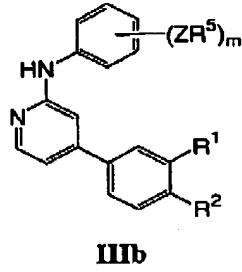
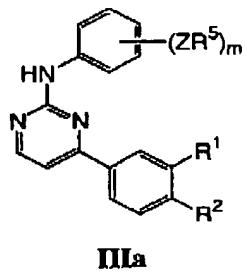


IIb

or a pharmaceutically acceptable salt thereof.

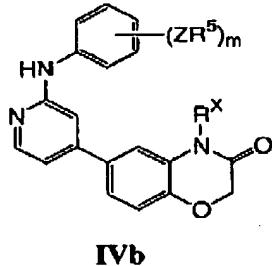
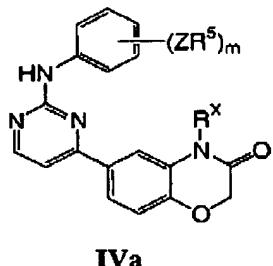
17. (Previously presented) The compound of claim 16, wherein R^3 is hydrogen, and compounds have the structure of Formula IIIa or IIIb:

Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



or a pharmaceutically acceptable salt thereof.

18. (Previously presented) The compound of claim 16, wherein R³ is hydrogen, and R¹ and R² taken together form the heterocyclic moiety of formula (a) and compounds have the structure of Formula IVa or IVb:



or a pharmaceutically acceptable salt thereof.

19. (Previously presented) The compound of claim 15, wherein
 i) R¹ and R² taken together form the heterocyclic moiety of formula (a); where R^X is defined according to one of the following groups:
 (a) hydrogen or optionally substituted C₁₋₆aliphatic;
 (b) hydrogen, methyl, ethyl, propyl, n-butyl, tert-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, C₁₋₆alkyl substituted with N(R)₂, or C₁₋₆alkyl substituted with Ar¹; or

Applicants: Randy S. Bethel et al.
Application No.: 10/700,936

(c) hydrogen, methyl, or C₁₋₂alkyl substituted with a group selected from optionally substituted phenyl, pyridyl, morpholino, piperidinyl, or piperazinyl.

ii) R³ is defined according to one of the following groups:

(a) hydrogen, halogen, QR or QAr¹, wherein Q is a C₁₋₃ alkylidene chain wherein one methylene unit of Q is optionally replaced by -O-, -S-, -NHCO-, or -NR-, and Ar¹ is an optionally substituted 5-6 membered saturated,

partially unsaturated, or fully unsaturated ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

(b) hydrogen, OH, OCH₃, OCH₂CH₃, NHCOMe, NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, O(CH₂)₂morpholin-4-yl, O(CH₂)₂NH₂, O(CH₂)₂NH(C₁₋₄ aliphatic), O(CH₂)₂N(C₁₋₄ aliphatic)₂, bromo, chloro, or fluoro; or

(c) hydrogen;

iii) R⁴ is defined according to one of the following groups:

(a) a 6-membered saturated, partially unsaturated, or aryl ring having 0-3 nitrogens, a 9-10 membered bicyclic aryl ring having 0-2 nitrogens, or a 5 membered heteroaryl ring having 2-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is optionally substituted with (ZR⁵)_m;

(b) an optionally substituted ring selected from phenyl, cyclohexyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, thiazolyl, thiadiazolyl, pyrazolyl, isoxazolyl, indazolyl, or benzimidazolyl, wherein said ring is optionally substituted with (ZR⁵)_m; or

(c) an optionally substituted phenyl group, wherein said phenyl group is optionally substituted with (ZR⁵)_m;

iv) W¹, W² and W³ are defined according to one of the following groups;

(a) W¹ is nitrogen or CH, W² is nitrogen or C-(U)_pR⁴, and W³ is nitrogen or C-(V)_qR⁵;

Applicants: Randy S. Bethel et al.
Application No.: 10/700,936

(b) W^1 is nitrogen or CH, W^2 is $C-(U)_pR^U$, and W^3 is $C-(V)_qR^V$; or
(c) W^1 is nitrogen or CH and W^2 and W^3 are each CH; and
v) $(U)_pR^U$ and $(V)_qR^V$ groups are defined according to one of the following groups:
(a) hydrogen, halogen, NO_2 , CN, OR, SR or $N(R)_2$, or C_{1-4} aliphatic
optionally substituted with oxo, OR, SR, $N(R)_2$, halogen, NO_2 or CN;
(b) hydrogen, Me, OH, OMe or $N(R)_2$; or
(c) both $(U)_pR^U$ and $(V)_qR^V$ are hydrogen.

20. (Previously presented) The compound of any one of claims 16, 17, 18 or 19, wherein each occurrence of Z is independently a bond or a C_{1-4} alkylidene chain wherein one methylene unit of Z is optionally replaced by -O-, -S-, - SO_2 -, or -NH-; and each occurrence of R^5 is independently hydrogen, C_{1-6} aliphatic, halogen, NO_2 , OR, $N(R)_2$, or optionally substituted phenyl, pyridyl, and pyrimidinyl.

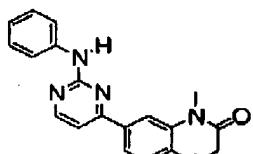
21. (Previously presented) The compound of claim 20, wherein each occurrence of ZR^5 is independently Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF_3 , NH₂, phenyl, benzyl, benzyloxy, OH, methylenedioxy, SO_2NH_2 , CONH₂, CO_2Me , phenoxy, O-pyridinyl, SO_2 phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF_3 -phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, or fluorophenoxy.

22. (Previously presented) The compound of claim 18 having the formula IVa, wherein R^X is hydrogen or optionally substituted C_{1-6} aliphatic; m is 0, 1 or 2; and ZR^5 is Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF_3 , NH₂, phenyl, benzyl, benzyloxy, OH, methylenedioxy, SO_2NH_2 , CONH₂, CO_2Me , phenoxy, O-pyridinyl, SO_2 phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF_3 -phenyl.

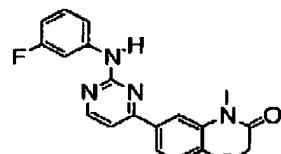
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936

dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, or fluorophenoxy.

23. (Previously presented) The compound of claim 1, selected from one of the following compounds:



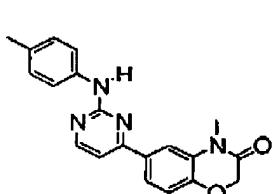
IVa-1



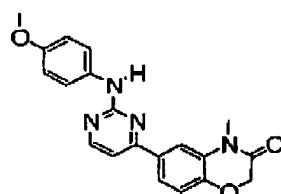
IVa-2



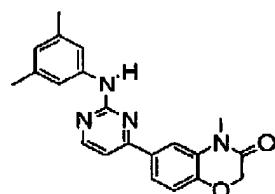
IVa-3



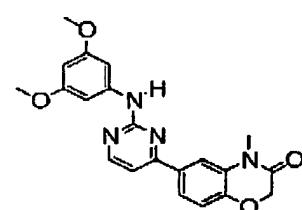
IVa-4



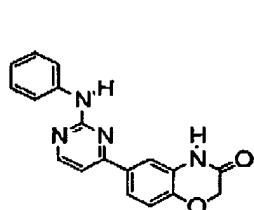
IVa-5



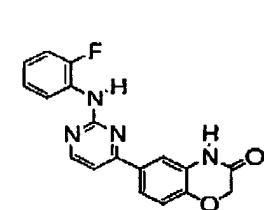
IVa-6



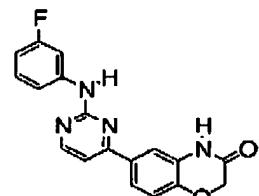
IVa-7



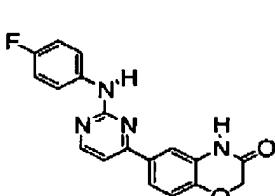
IVa-8



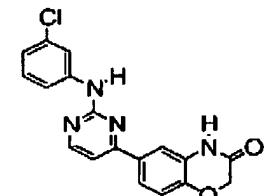
IVa-9



IVa-10

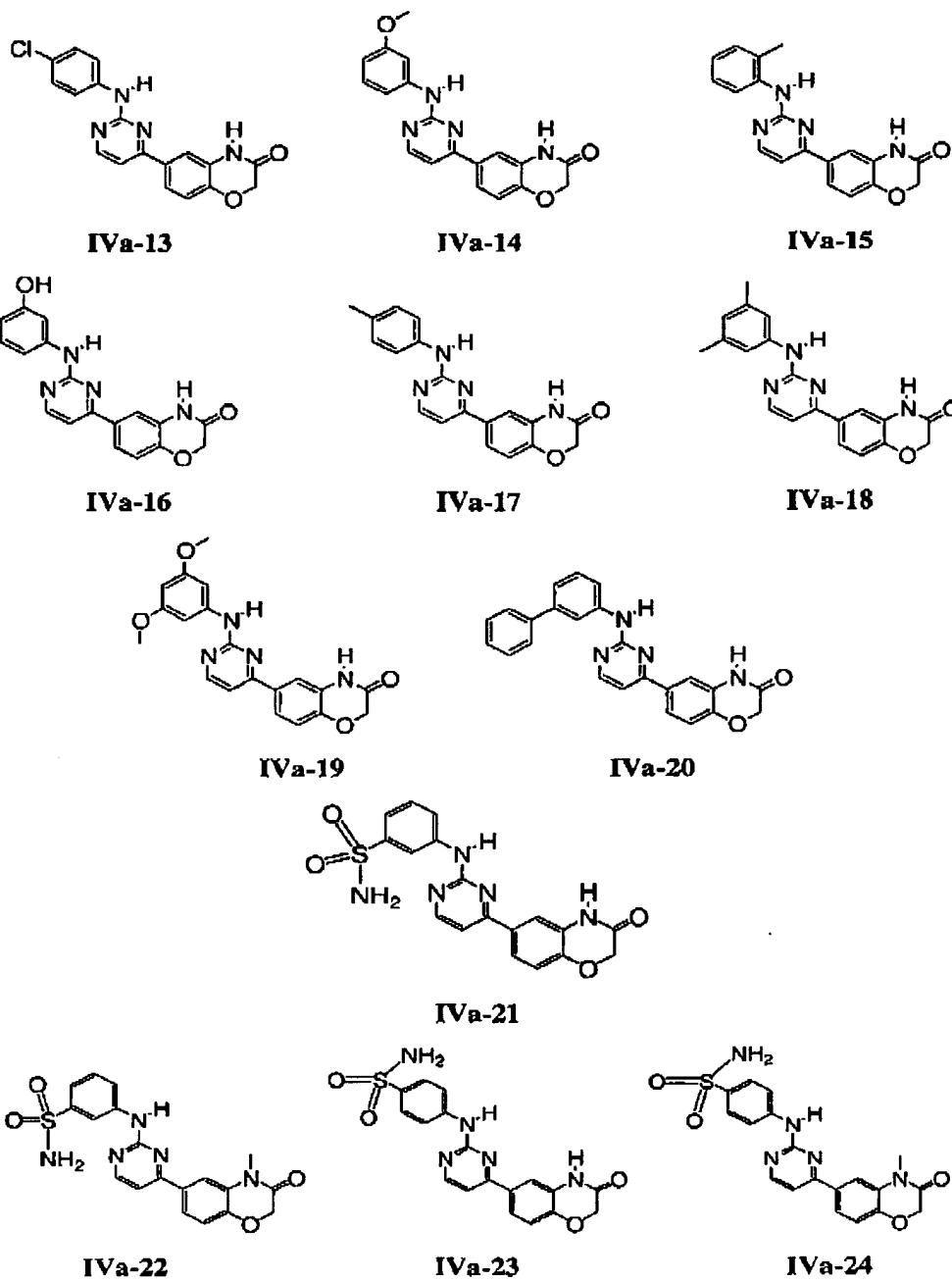


IVa-11

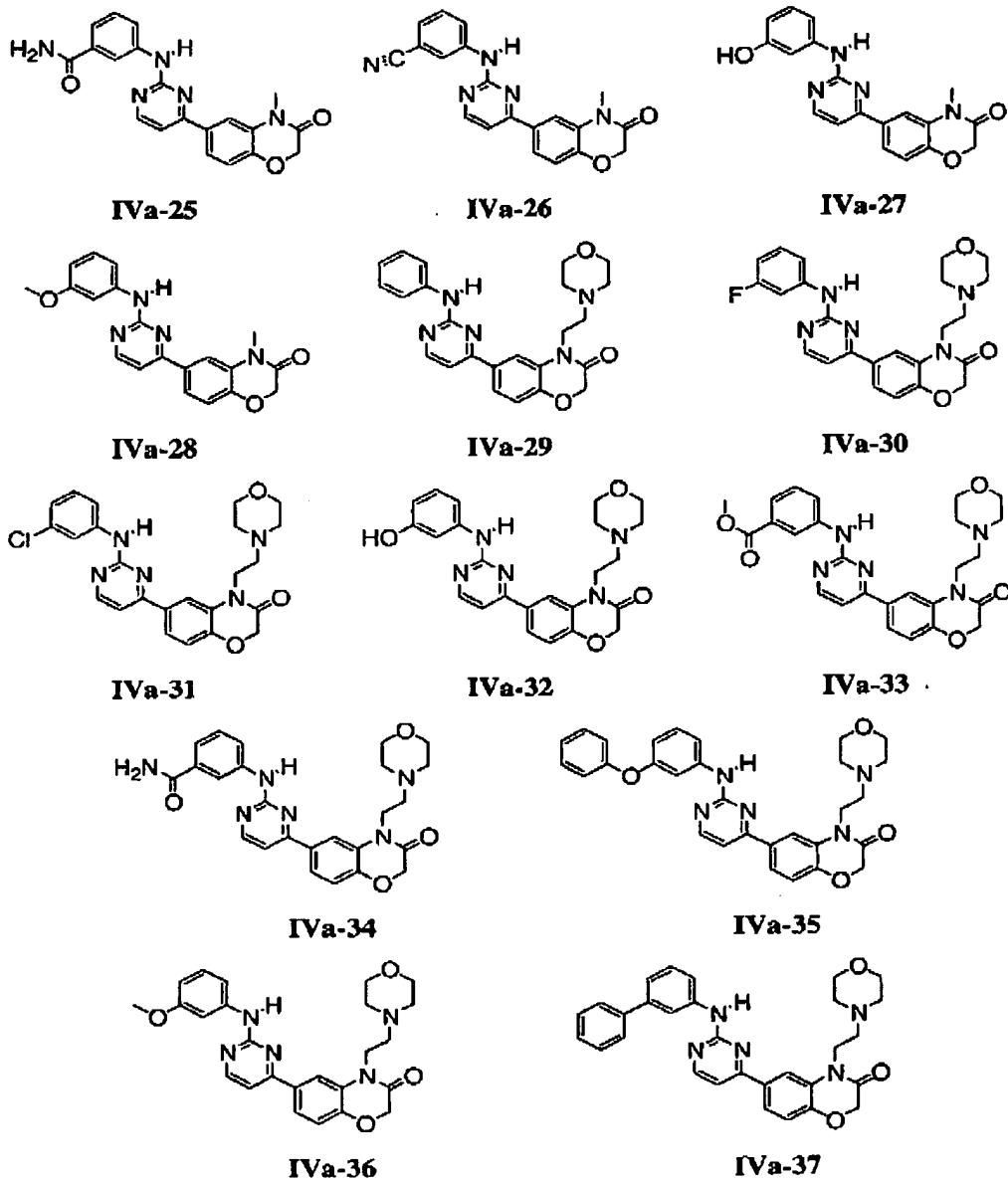


IVa-12

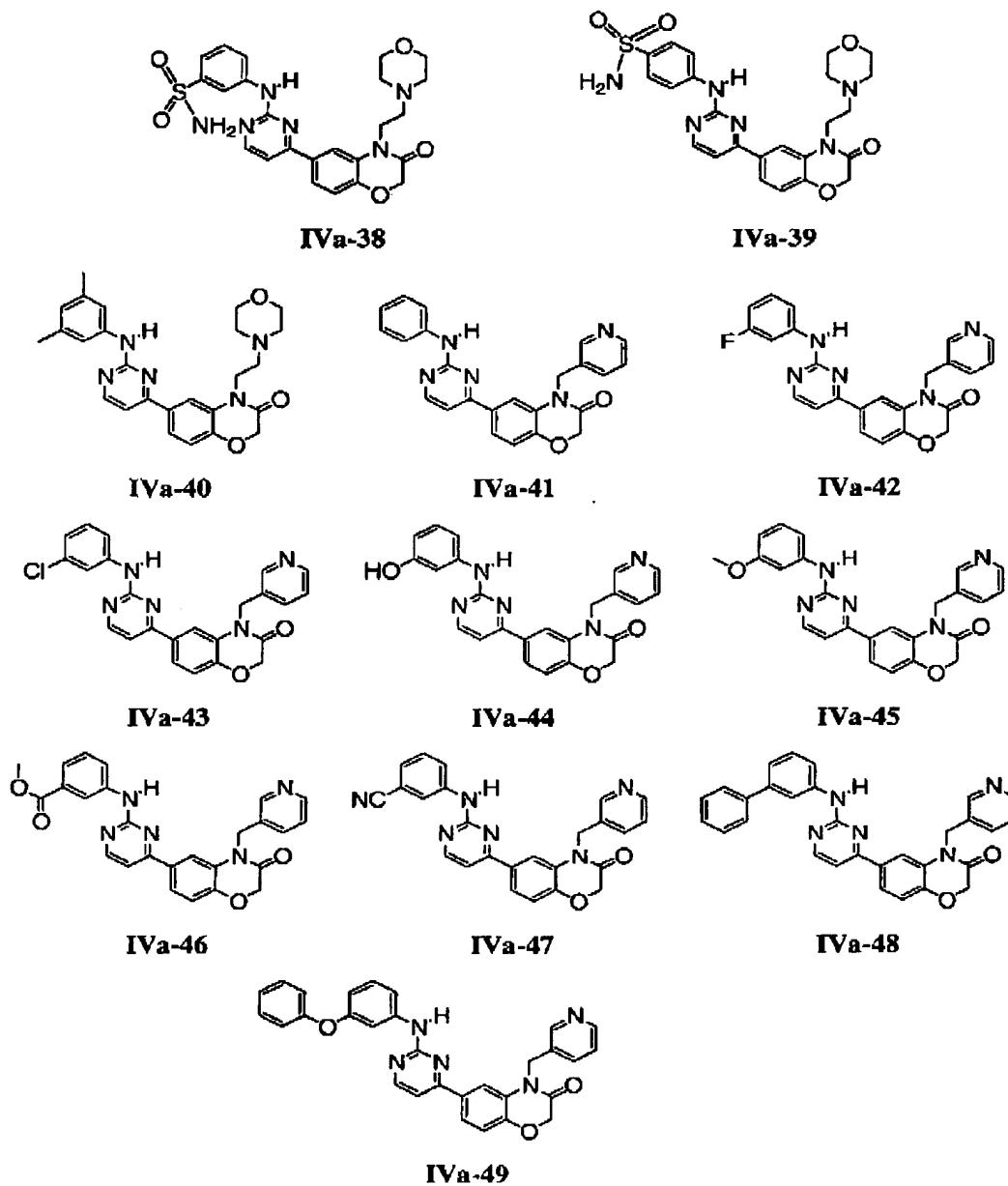
Applicants: Randy S. Bethel et al.
Application No.: 10/700,936



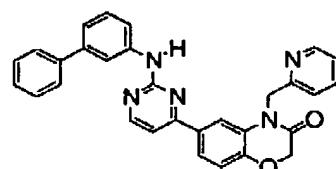
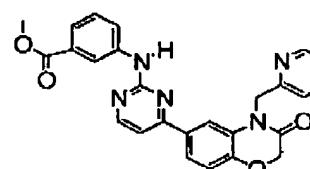
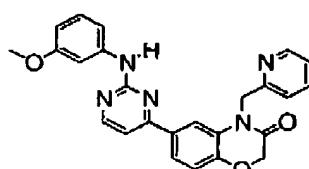
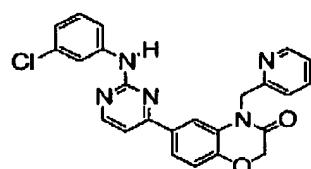
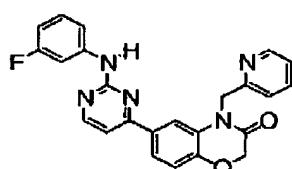
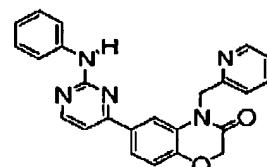
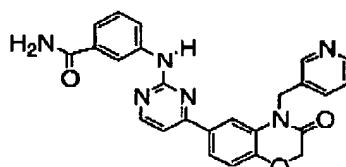
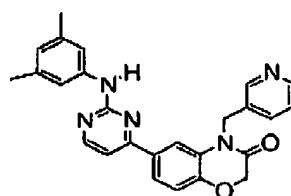
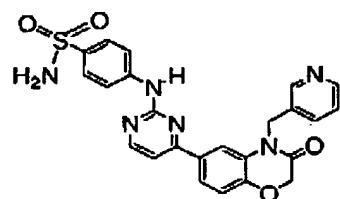
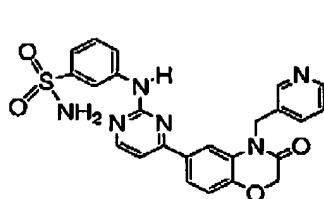
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



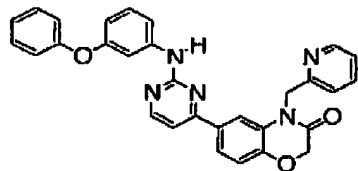
Applicants: Randy S. Bethel et al.
Application No.: 10/700,936



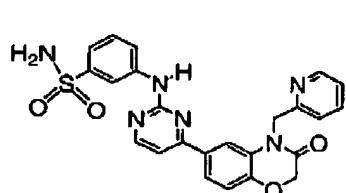
Applicants: Randy S. Bethel et al.
Application No.: 10/700,936



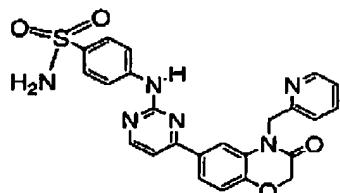
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



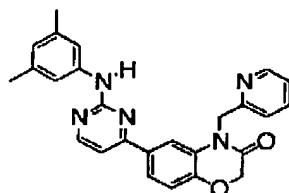
IVa-60



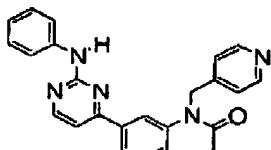
IVa-61



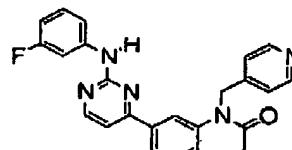
IVa-62



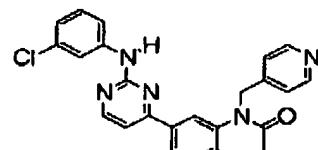
IVa-63



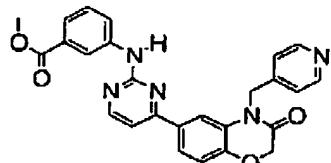
IVa-64



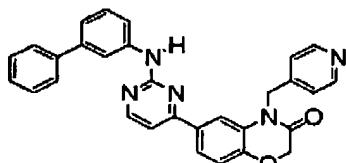
IVa-65



IVa-66

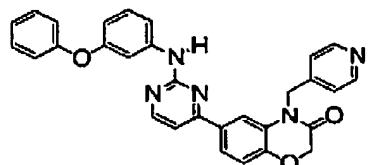


IVa-67

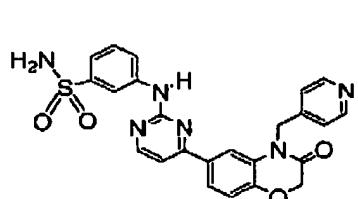


IVa-68

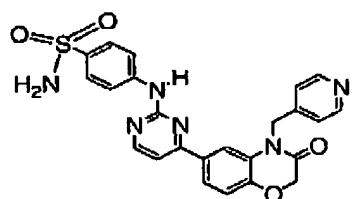
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



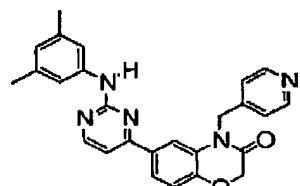
IVa-69



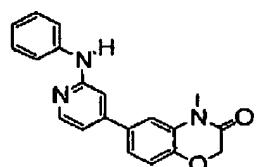
IVa-70



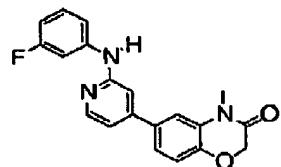
IVa-71



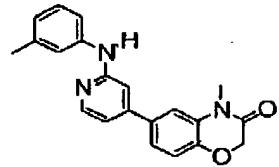
IVa-72



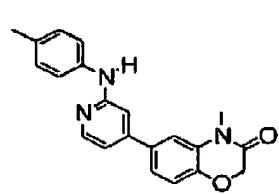
IVb-1



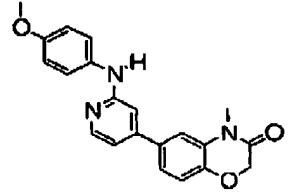
IVb-2



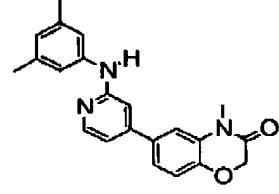
IVb-3



IVb-4

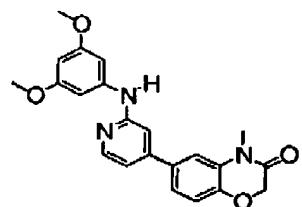


IVb-5

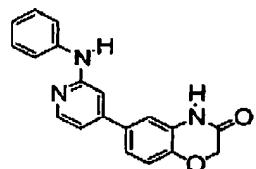


IVb-6

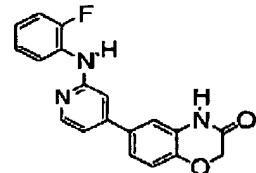
Applicants: Randy S. Bethel et al.
Application No.: 10/700,936



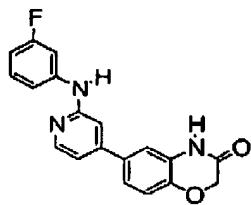
IVb-7



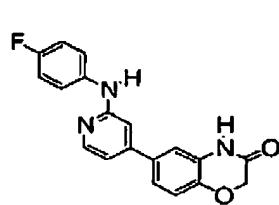
IVb-8



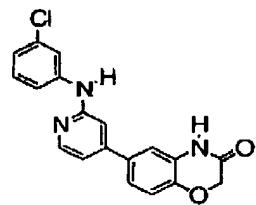
IVb-9



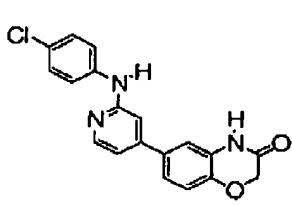
IVb-10



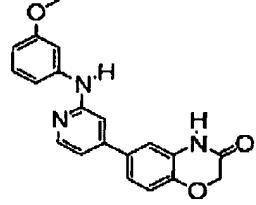
IVb-11



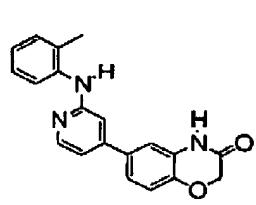
IVb-12



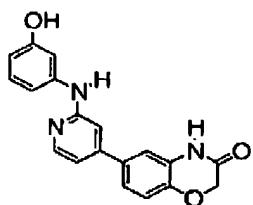
IVb-13



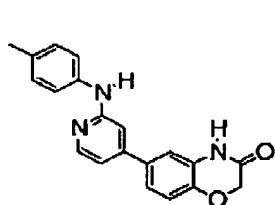
IVb-14



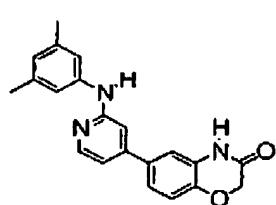
IVb-15



IVb-16

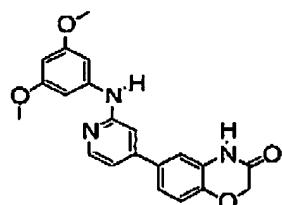


IVb-17

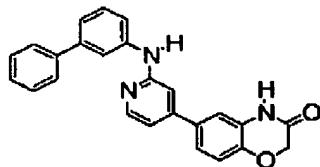


IVb-18

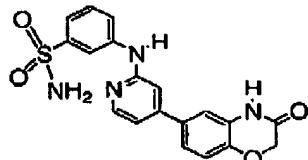
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



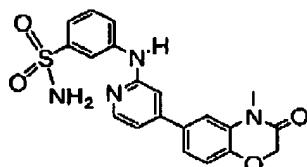
IVb-19



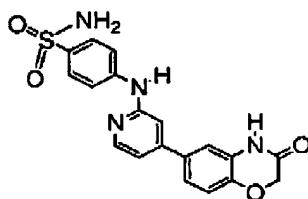
IVb-20



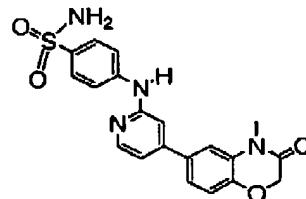
IVb-21



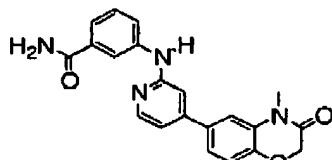
IVb-22



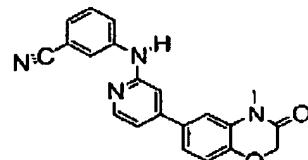
IVb-23



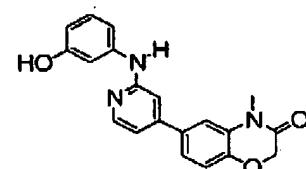
IVb-24



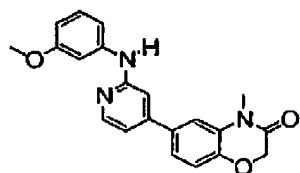
IVb-25



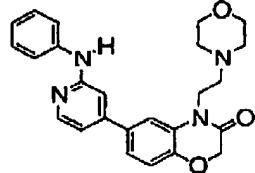
IVb-26



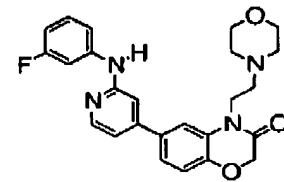
IVb-27



IVb-28

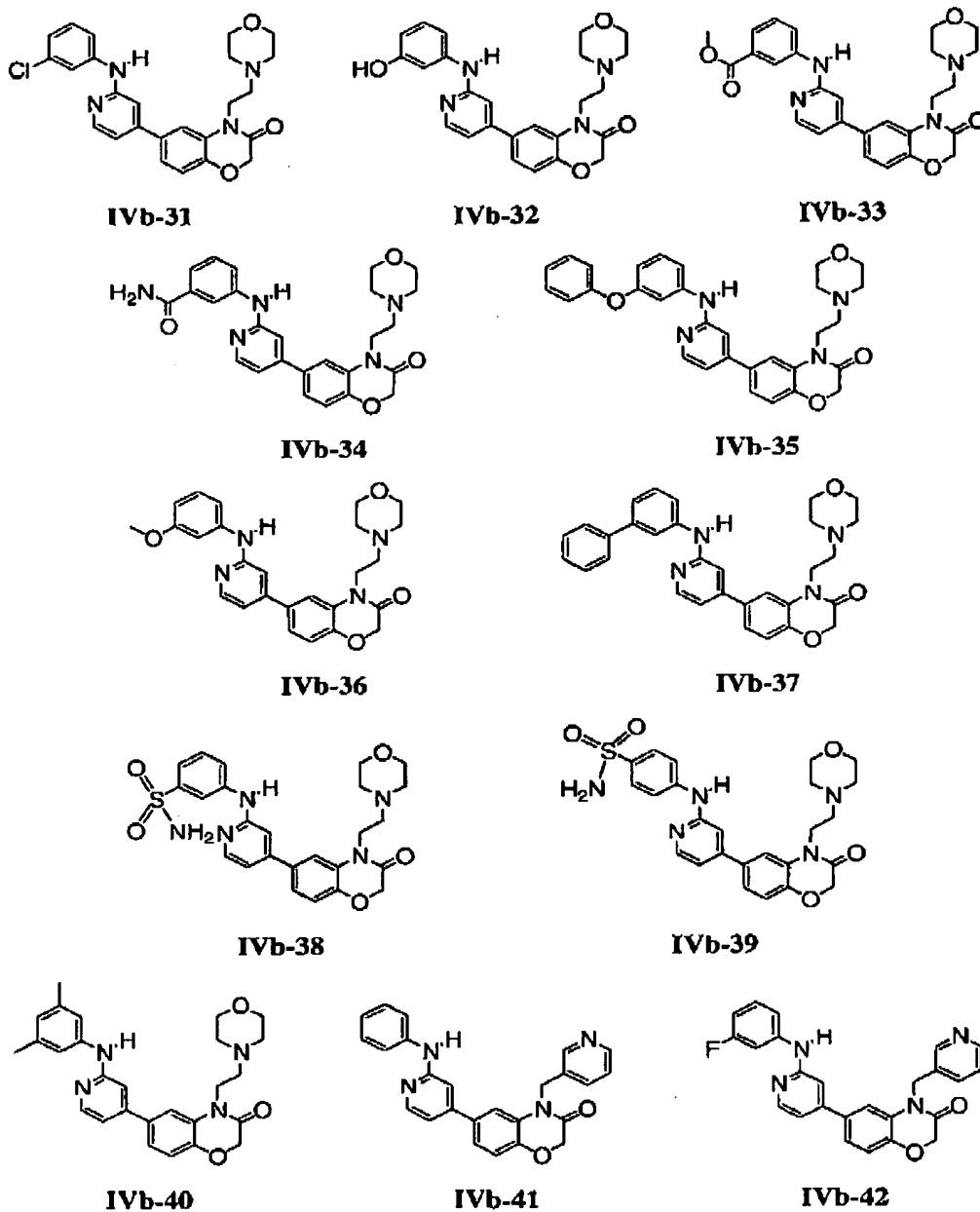


IVb-29

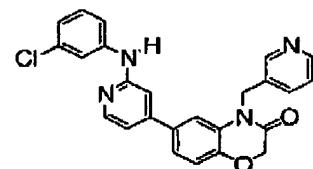


IVb-30

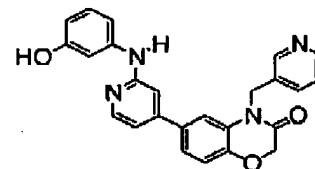
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



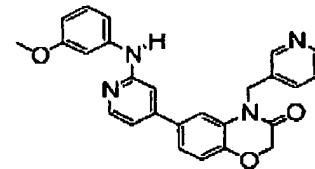
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



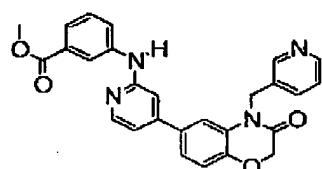
IVb-43



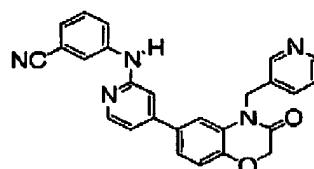
IVb-44



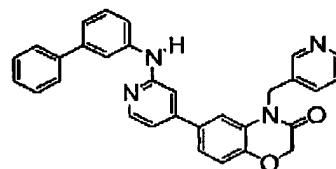
IVb-45



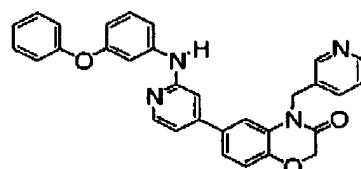
IVb-46



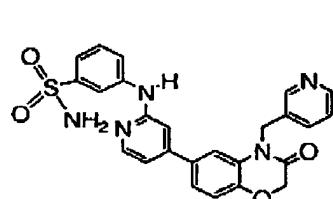
IVb-47



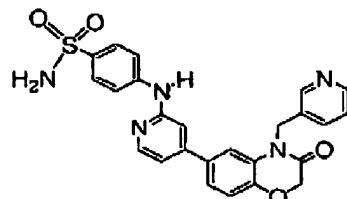
IVb-48



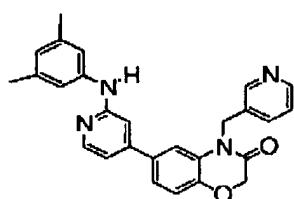
IVb-49



IVb-50

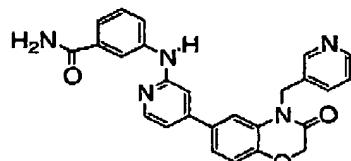


IVb-51

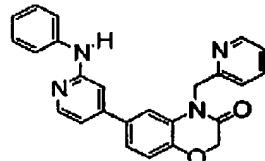


IVb-52

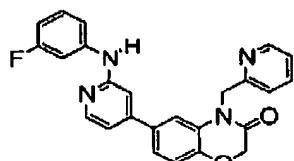
Applicants: Randy S. Bethel et al.
Application No.: 10/700,936



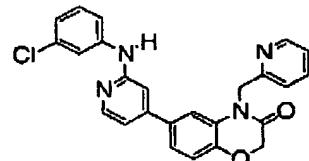
IVb-53



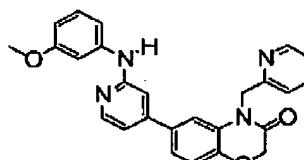
IVb-54



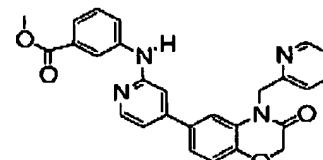
IVb-55



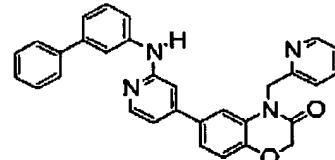
IVb-56



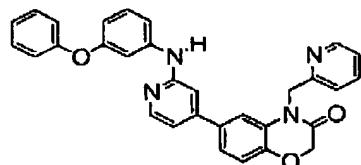
IVb-57



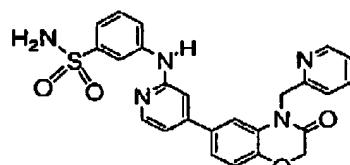
IVb-58



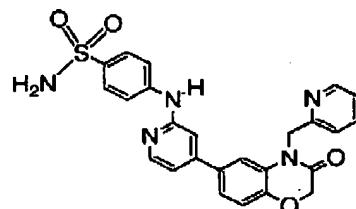
IVb-59



IVb-60

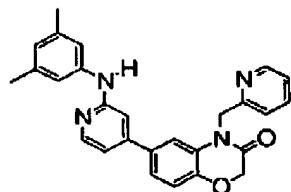


IVb-61

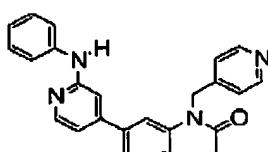


IVb-62

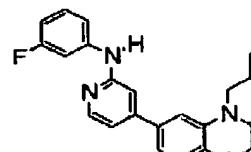
Applicants: Randy S. Bethel et al.
Application No.: 10/700,936



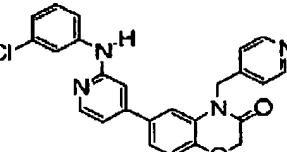
IVb-63



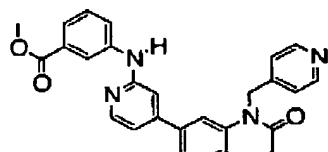
IVb-64



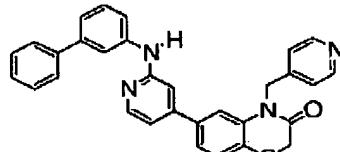
IVb-65



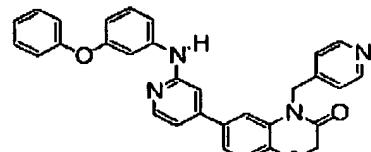
IVb-66



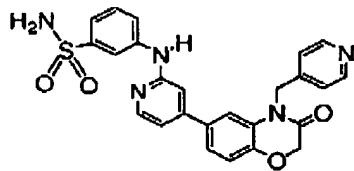
IVb-67



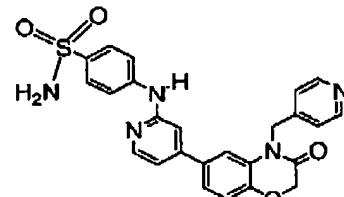
IVb-68



IVb-69

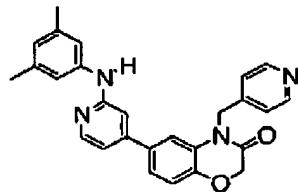


IVb-70



IVb-71

Applicants: Randy S. Bethel et al.
Application No.: 10/700,936



or IVb-72.

24. (Original) A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

25. (Canceled)

26. (Currently amended) A method of inhibiting JAK-3 kinase activity in a biological sample; [f:]

- (a) a patient; or
- (b) a biological sample;

which method comprises ~~administering to said patient, or contacting said biological sample with a compound of claim 1 or a composition comprising said compound.~~

27. (Canceled)

28. (Currently amended) A method of treating or lessening the severity of a disease or disorder selected from an allergic or type I hypersensitivity reaction, asthma, transplant rejection, graft versus host disease, rheumatoid arthritis, amyotrophic lateral sclerosis, multiple sclerosis, Familial amyotrophic lateral sclerosis (FALS), or leukemia, or lymphoma comprising administering to a subject in need thereof a compound of claim 1 or a composition comprising said compound.

Applicants: Randy S. Bethel et al.
Application No.: 10/700,936

29. (Currently amended) The method of claim 28, comprising the further step of administering to said patient an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, ~~a treatment for Alzheimer's Disease, a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an agent for treating schizophrenia, an anti-inflammatory agent, or an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an agent for treating a blood disorder, or an agent for treating an immunodeficiency disorder,~~ wherein:

said additional therapeutic agent is appropriate for the disease being treated; and
said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.